REMARKS

Applicants have amended claim 1; cancelled claim 2; and withdrawn claims 6-17 as directed to non-elected subject matter. Representative support for present amendments may be found in original claim 2 and in the specification at page 5, lines 1-10. Accordingly, claims 1 and 3-5 are pending in this patent application.

Rejection under 35 U.S.C. § 112 (Enablement)

Claims 1 and 3-5 stand rejected for allegedly failing to satisfy the enablement requirement under 35 U.S.C. § 112 (1st). The Examiner states that the application enables a method of treating patients who have diseases characterized by bone loss comprising administering an amount of TRANCE/RANK inhibitors, wherein the inhibitors are selected from known TRANCE/RANK inhibitors of the prior art. Office Action, at 2. In particular, the Examiner acknowledges that Applicants have provided sufficient support for a method of treating bone loss using a peptidomimetic (WP9QY) and osteoprotegerin. *Id.*, at 7. The Examiner asserts, however, that with regard to the TRANCE/RANK inhibitors of Formula I, including particular species IA, the claims are allegedly not enabled. *Id.*, at 2-3. The primary basis for the Examiner's assertion appears to be the absence of working examples using the TRANCE/RANK inhibitors of Formula I. *Id.*, at 4, 7. Likewise, the Examiner relies on the absence of any small molecule TRANCE/RANK inhibitors in the prior art as rendering the instant claims allegedly non-enabled. *Id.*, at 7. Thus, according to the Examiner, the claims are not enabled because it would take undue experimentation to practice the instant claims. *Id.*, at 3.

Applicants respectfully disagree with the Examiner's enablement assessment with respect to the TRANCE/RANK inhibitors of Formula I. In making a determination of enablement, the inquiry is not whether experimentation is required, but rather whether the experimentation required is undue. According to the Federal Circuit, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed . . . ." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (citations omitted). In *In re Wands*, eight factors to be considered in assessing whether a

disclosure is enabling were elucidated: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Thus, a patent claim is invalid for lack of enablement in instances in which consideration of the Wands factors leads to a conclusion that practice of the invention would require undue experimentation.

Applicants assert that the Examiner places too much reliance on the absence of a working example – only one of the *Wands* factors – to allegedly defeat the enablement of the instant claims. *See* MPEP 2164.02 (describing how an otherwise enabled invention should not be rejected for lacking a working example). The Examiner states that the application enables a method of treating patients who have diseases characterized by bone loss comprising administering an amount of TRANCE/RANK inhibitors, wherein the inhibitors are selected from known TRANCE/RANK inhibitors of the prior art, such as polypeptides and anti-sense molecules. Office Action, at 2, 5-7. Therefore, the only allegedly missing component of the instant application appears to be a working example using the small molecule of Formula I. This is not a sufficient basis for rejecting the instant claims.

The other *Wands* factors support the position that the instant claims are enabled. In the present case, the skill in the art of signal transduction is high and the state of that art is sufficiently developed such that one skilled in the art, armed with the detailed teachings of the present specification and the working examples provided therein, would be able to make and use the presently claimed invention with no more than routine experimentation.

Regarding the nature of the invention, the Applicants agree that it relates to a method of treating patients who have diseases characterized by bone loss comprising administer an amount of TRANCE/RANK inhibitors effective to inhibit osteoclastogenesis and/or osteoclast function. *Id.*, at 4. Examiner asserts that the nature of the claimed invention is enabled with respect to TRANCE/RANK inhibitors in the prior art. *Id.*, at 3.

Regarding the breadth of the claims, Applicants disagree with the Examiner's characterization of the claims. *Id.*, at 4. As pending the claims are direct to methods using compounds of Formula I. Regarding guidance in the specification, the application discloses many compounds, their sources, and methods of formulating and administering that are

known in the art. Specification, at 5-6, 12-16. As the Examiner knows, the patent should exclude what is well known in the art. *See* MPEP 2164.01.

Apart from using small molecules to inhibit TRANCE/RANK inhibitors, the Examiner appears to agree that the claims are enabled. Regarding the state and predictability in the art, Examiner identified a number of papers which, according to the Examiner, demonstrate using polypeptides and anti-sense TRANCE/RANK inhibitors for treating patient who have conditioned characterized by bone. Whereas these papers rely upon compositions – polypeptides and anti-sense nucleotides – that are relatively recent additions to the repertoire of compounds available to therapeutic use generally. If the prior art are enabling for these arguably unpredictable and new compounds, it must be the case that Applicants have satisfied using a small molecule, which are staples of human medicine. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 102 (b)

Claim 1 is rejected as being allegedly anticipated by Boyle et al. (EP0784093). Applicants agree with the Examiner that Boyle describes methods of treating various bone diseases using either polypeptide, anti-sense technology, or gene therapy. Accordingly, Boyles does not disclose every element of claim 1, and therefore fails to anticipate claim 1. Applicants respectfully request withdrawal of this rejection.

Conclusion

Favorable consideration and an early notice of allowance are earnestly solicited. If the Examiner believes that a telephone conversation would further the prosecution of this case, he is invited to telephone the undersigned at his convenience.

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